April 14, 1949.

Dr. David M. Bonner,
Osborn Botanical Laboratory,
Yale University,
New Haven, Connecticut.

Dear Dave:

I was glad to hear that Landman has gotten so far in the purification of Neurospora lactase. What's the latest on it? We haven't been so ambitious; I haven't even given very much thought to the possibility, on purely a priori discouragements. It's a little harder to collect a kilo of dry E. coli than of Neurospora. But it has turned out to be so easy to extract, with water from cells dried over P_2O_5, that I may give a try at chromatographic separation, with ONPG as an indicator. By the way, your letter of Febr. 24 mentioned that you might be able to spare some ONPG. Our supplies are getting low, and I would be grateful for any amount that you can comfortably divert.

It would be interesting to compare some of your purified Neurospora lactase kinetically with our coli preps. Can you send some? I am sending along 100 mg. active dry cells of K-12 for you to play with. The powder should be triturated suspended in 10 ml water, and after shaking a couple of hours, sedimented at ca. 3500 rpm: 20 mins to prepare the extract. You should get an activity of about 100 u./ml, a unit being the amount of enzyme which splits enough ONP from excess ONPG in a volume of 10 ml. to cause a deflection of 10 optical density units in the Coleman spectrophotometer. This is just a lab unit; sometime I'll recalculate it kinetically.

I think we have found a different enzyme (not just presence or absence) in one of the mutant-suppressor combinations. (Lac_1^- - $Supp_{L1}^{+/-}$). It seems to be distinguished from wild type by a K_{onpg} of 7.7×10^{-4}, compared with 1.3×10^{-4} for $Lac_1^{+/-}$. But I wouldn't put any heavy interpretations on this. You can't distinguish an enzyme whose specificity has been "altered by a gene", from just another enzyme which does the same job. Lac_1^- does produce the "type" galactosidase under certain conditions, so one can regard the determination of the different K_m as a one-gene affair ($Supp_{L1}^{-/+}$).

The heterozygotes are no less puzzling than in November. A lot more linkage data, but it doesn't point to anything simpler than some kind of aberration. I have a paper in press in PNAS, in which I expressed the fearful possibility that the same kind of aberration might operate in the formation of "normal" prototrophs. But there are large discrepancies in the linkage relationships that mitigate against this. Zelle has been single-celling them, and confirms their one-cell origin. His pedigrees so far haven't shown much more, but this seems to be the most promising approach.

Something else has come up that may amuse you, as it has distracted me. K-12 is lysogenic. The phage that it carries symbiotically, however, has so far attacked only two coli strains that were obtained as "mutants" from K-12. These mutants are probably merely cultures which have been disinfected by ultra-violet light, and accordingly become susceptible. They can be reinfected to become lysogenic again. This has absolutely nothing whatever to do with recombination, but it does have "plasmagene" significance, as the symbiosis conditions, by "interference" resistance to two phages, p19 and p20 that were picked from Madison and Chicago sewage for this purpose. I have been surprised to hear the suggestion (revived from the literature of 30 years ago) that the lysogenic phage is a sort of gamete since it has a tail!

Any chance of seeing you in Detroit? or Cincinnati?

Best regards